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Streamlined Biosimilar Development
Key developments in the last 12 months

AAM GRx + Biosims Conference 2025
27-29 October 2025, Bethesda

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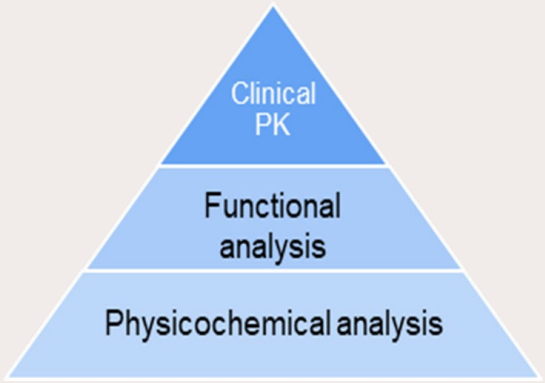
Streamlined Biosimilar Development
Key regulatory actions in the last 12 months



FDA started to agree on streamlined development proposals without a comparative efficacy study [1, 2]

A breakthrough moment for streamlined biosimilar development

1. Press release Feb 2025, https://www.formycon.com/en/blog/press-release/formycon-ag-informs-about-recent-developments-in-various-biosimilar-projects-and-invites-to-conference-call/
2. Generics Bulletin May 2025, https://insights.citeline.com/generics-bulletin/products/biosimilars/sandoz-slims-down-pembrolizumab-trial-as-regulators-streamline-requirements-G45RBFX6XFGV5KQS2M2IQ56O3E/

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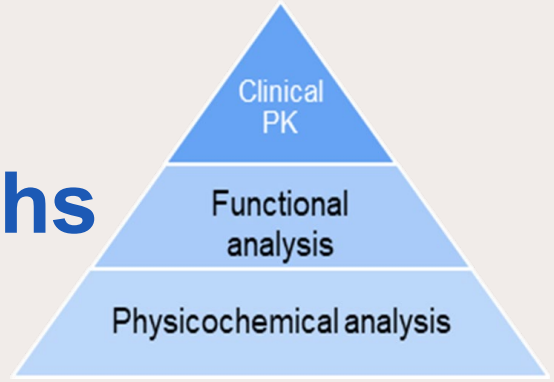
Streamlined Biosimilar Development
Key guideline developments in the last 12 months



Guideline Development

- Health Canada published draft guideline with the future-proof concept to reverse the burden of proof for the absence of a Comparative Efficacy Study [1]
  - *"The clinical studies required to support the authorization of a biosimilar are generally limited to a comparative pharmacokinetic trial …"*
  - *"If a comparative clinical efficacy and safety trial(s) is deemed necessary, sponsors should provide a rationale to explain the purpose of the trial(s) in the context of a biosimilar submission."*
- EMA is working on a reflection paper on streamlining and hosted major workshop on September [2]
- ICH has started guideline development on "Framework for Determining Utility of Comparative Efficacy Studies in Biosimilar Development Programs" [3]

- **Streamlined biosimilar development may become the new default.**
- **The ICH imitative will greatly facilitate global harmonization.**

1. Health Canada 2025, Link to draft guidance – here –
2. EMA 2025, https://www.ema.europa.eu/en/events/workshop-tailored-clinical-approach-biosimilar-development
3. ICH 2025, https://admin.ich.org/sites/default/files/2025-06/ICH%20Assembly%20Madrid%20Meeting%2C%2013-14%20May%202025.pdf

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New studies on the role of safety and immunogenicity data of clinical pharmacokinetic studies

FDA authors:

- Ji P, Schrieber SJ, Glaser R, Chen J, Shukla C, Doddapaneni S, Chandrahas S
  A Meta-Analysis of the Safety and Immunogenicity of Pharmacokinetic Similarity Studies and Comparative Clinical Studies [1]
  - "***Pharmacokinetic similarity studies, as currently designed, provide useful information to descriptively evaluate immunogenicity and safety, and comparative clinical [efficacy] studies do not appear to be more definitive***."

Industry authors:

- Schiestl M, Roy N, Trieb M, Park JP, Guillen E, Woollett G, Wolff-Holz E
  Analytical Data and Single-Dose PK are Sufficient to Conclude Comparable Immunogenicity for Biosimilars: An Ustekinumab Case Study [2]

Clinical pharmacokinetic studies as currently designed are sufficient for streamlined biosimilar development

1. Ji et al, J. Clin. Pharmacol. 2025;65(4) 499–507. https://doi.org/10.1002/jcph.6165
2. Schiestl et al, BioDrugs 2025;39;769-776. https://doi.org/10.1007/s40259-025-00733-1

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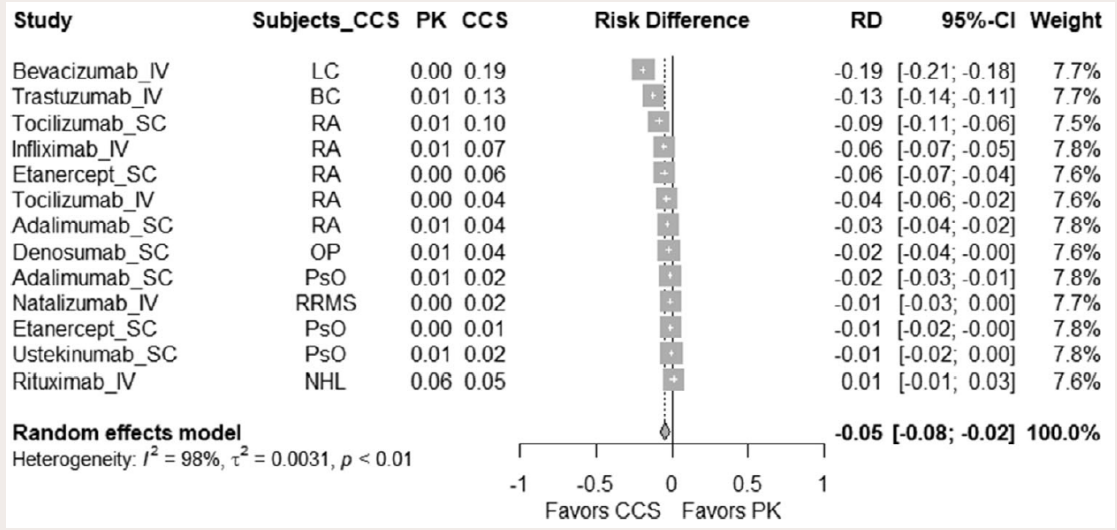
Ji et al.: Comparison of descriptive safety data between pharmacokinetic and comparative efficacy studies [1]

Serious Adverse Events



Anti-drug antibody incidence

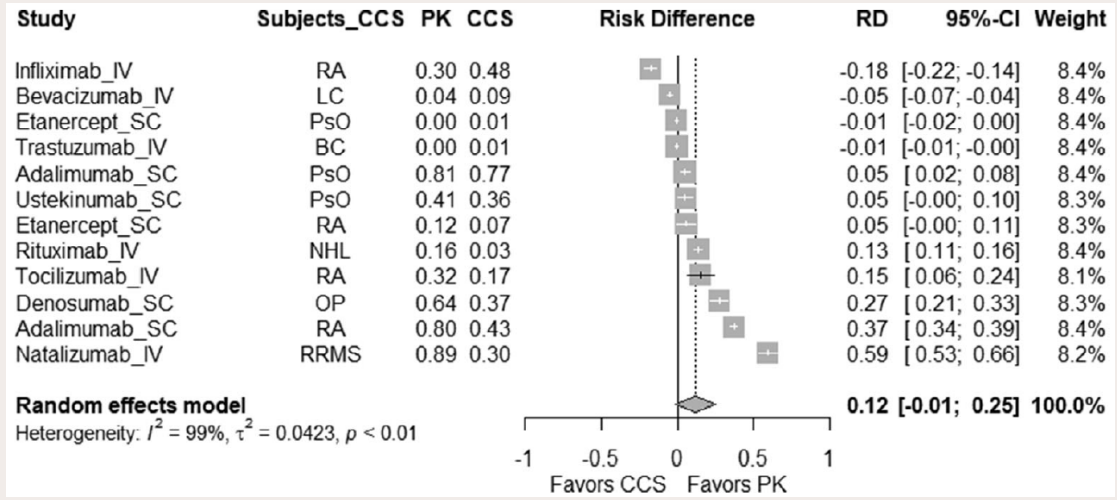


Illustration of risk differences in proportion of subjects between pharmacokinetic studies (PK) and comparative clinical [efficacy] studies (CCS).

"While there were numerical differences in the average risk difference for AEs, serious AEs, AEs leading to discontinuation, and deaths, the trend is consistent, indicating fewer subjects experienced these AEs across all categories in the PK studies compared to the CCS."

"The overall risk difference (95% CI) for ADA incidence is 0.12 [-0.01,0.25], indicating that ADA development in pharmacokinetic similarity studies is not less compared to CCS."

1. Ji et al, J. Clin. Pharmacol. 2025;65(4) 499–507. https://doi.org/10.1002/jcph.6165

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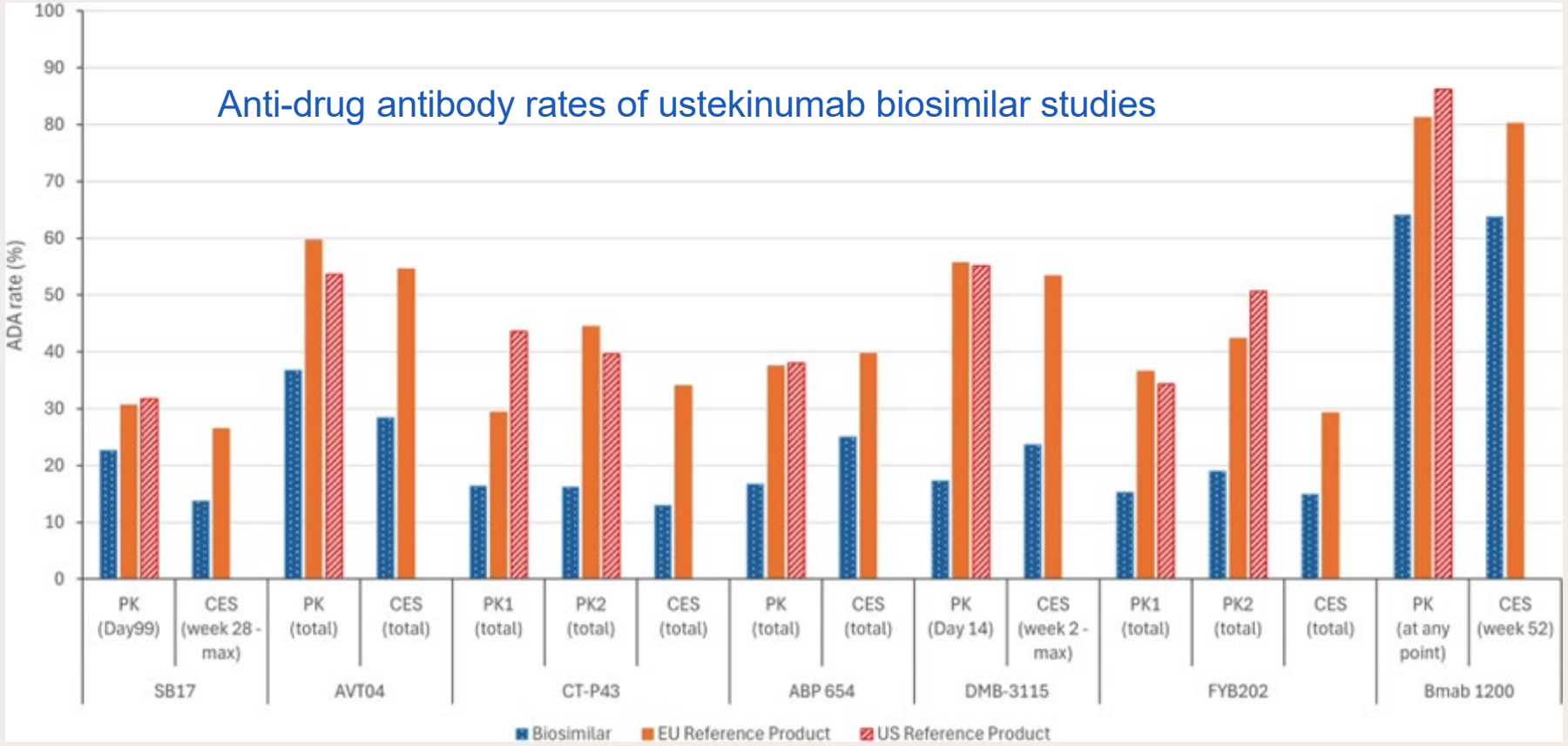
Ustekinumab case study: Comparison of immunogenicity data between pharmacokinetic and comparative efficacy studies [1]



Single dose PK studies in healthy volunteers revealed a numerically lower immunogenicity of Ustekinumab biosimilar medicines compared to the reference product.

Anti-drug antibody values depend on the assay sensitivity of the respective study

The Anti-drug antibody incidences found in the PK study were reproduced in the CES studies. CES did not provide further insights.

1. Schiestl et al, BioDrugs 2025;39;769-776. https://doi.org/10.1007/s40259-025-00733-1

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Thank you all

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